

TEXAS MEDICAL CENTER NASA/JOHNSON SPACE CENTER
COOPERATIVE AGREEMENT PROGRAM NCC 9-36, ROUND II

COVER SHEET FOR FINAL REPORT

Please follow this format:

1N-52
026 069

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Title: Professor of Otolaryngology and Director of Research

Institution: University of Texas Houston Health Science Center

Name of Project: MAPS of Cancer

Amount of Grant:

~~XXXXXX~~

* Amount Spent, if Different from Amount Granted:

Date Project Was Completed:

6/30/98

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MAPS OF CANCER

NASA/TMC Final Project Report

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Accomplishment of Stated Goal:

Our goal was to produce an interactive visualization from a mathematical model that successfully predicts metastases from head and neck cancer. We met this goal early in the project. The visualization is available for the public to view at <http://oto.med.uth.tmc.edu>. This web site gets about 80 hits a month with no active advertising, and the P.I. gets several email requests for more details. Our work appears to fill a need for more information about this deadly disease.

The idea of this project was to make an easily interpretable visualization based on what we call "functional maps" of disease. A functional map is a graphic summary of medical data, where distances between parts of the body are determined by the probability of disease, not by anatomical distances. Details of the algorithm can be found in Gray et al. (1993; Int. J. Supercomputer Applications 7:167). Functional maps often bear little resemblance to anatomical maps, but they can be used to predict the spread of disease. The idea of modeling the spread of disease in an abstract multidimensional space is difficult for many people. Our goal was to make the important predictions easy to see. NASA must face this problem frequently: how to help laypersons and professionals see important trends in abstract, complex data. We took advantage of concepts perfected in NASA's graphics libraries.

As an analogy, consider a functional map of early America. Suppose we chose travel times, rather than miles, as our measures of inter-city distances. For Abraham Lincoln, travel times would have been the more meaningful measure of separation between cities. In such a map New Orleans would be close to Memphis because of the Mississippi River. St. Louis would be close to Portland because of the Oregon Trail. Oklahoma City would be far from Little Rock because of the Cheyenne. Such a map would look puzzling to those of us who have always seen physical maps, but the functional map would be more useful in predicting the probabilities of inter-site transit. Continuing the analogy, we could predict the spread of social diseases such as gambling along the rivers and cattle rustling along the trails. We could simply print the functional map of America, but it would be more interesting to show meaningful patterns of dispersal.

We had previously published the functional map of the head and neck, but it was difficult to explain to either patients or surgeons because that view of our body did not resemble anatomy. This discrepancy between functional and physical maps is just a mathematical restatement of the well-known fact that some diseases, such as head and neck cancer, spread in complex patterns, not always to the next nearest site. We had discovered that a computer could re-arrange anatomy so that this particular disease spreads to the next nearest site. The functional map explains over 95% of the metastases in 1400 patients. In a sense, we had graphed what our body "looks like" to a tumor. The tumor readily travels between adjacent areas in the functional map. The functional map is a succinct visual display of trends that are not easily appreciated in tables of probabilities.

What we needed was a way to display the accurate predictions in a way that made sense to non-mathematicians. We did this through interactive visualization. From one menu you pick

where a cancer might start. From another menu you pick how far you think the disease might have spread. The program displays predicted metastases as changing colors on a realistic depiction of the body. The program is actually calculating an expanding ellipse in the space of the functional map. You can see this process by clicking the "Abstract Map" tab at the top of our new breast cancer visualization, which can be found at the bottom of our Web page.

The visualizations produced under this NASA/TMC contract allow people to see predictable patterns in different diseases. The programs are easy to use and contain no sensitive information or displays. They are appropriate for lay persons to look for general patterns and for physicians to look for specific details.

Extension of Goals:

By February 1997 we were satisfied that we had met the stated goal of our project and set out to extend the method. We found a collaborator who shared data on metastases from melanoma (the most rapidly increasing form of cancer in this part of the country). The mathematical modeling of melanoma was completed and then two different visualizations of this disease were programmed (but not yet made public because a scientific paper about the modeling has not yet been published). We will soon get access to more melanoma data and will probably submit a publication on a more thorough analysis and will then make the visualization public.

One potential use of functional mapping is to show subtly different patterns in different populations. To test this hypothesis, about 500 hospital medical records from Pakistan, India, and Egypt were examined. These data were used to make mathematical models of head and neck cancer in these developing countries. We were able to prove that the patterns of metastases, though similar everywhere in the world, are significantly different in different populations. An important humanitarian service could be provided through slight variations in our visualizations. Surgeons in developing countries could then see how the diseases they encounter are different than descriptions in standard texts (which, for the Indian and Pakistani physicians, are usually from U.S. or the U.K.).

At the same time we were describing significant functional differences in Asia and America, other scientists were proving that there are significantly different genetic mutations in India and the United States. The exciting suggestion of this congruence is that genetic differences lead to functional differences in patterns of metastases. This will become important as more genetic studies are done on tumors. That is, functional mapping will help us understand, possibly even predict, the behaviors of genetically different tumors.

Additional data from Asian colleagues have allowed analyses of breast cancer, tuberculosis in AIDS patients, and the growth of human cancers in mice (an animal model of oral tumors). The breast cancer visualization is currently available for viewing, below a disclaimer (because the paper on the analysis is not yet accepted for publication) on our Web page. These additional data are important because they show that the technique of functional mapping is applicable to a wide range of disease. Thus, progress in one problem will likely contribute to solutions for others.

Enclosed are examples of the three visualizations: head and neck cancer, melanoma, and breast cancer.

Deterrents and Obstacles:

The deterrents and obstacles to the work were few. We faced a slight challenge in readjusting our initial programming concepts to a new language, Java. The interactive visualizations have gone a long way toward convincing skeptics about the value of functional mapping.

Interest from the Public and Scientific Community:

Our Web site gets 80 "hits" a month. P.I. gets unsolicited email from all over the world about 10 times a year, asking about some detail.

Experienced surgeons find the displays consistent with what they know about these diseases. The displays can also teach or remind physicians about details they may have forgotten. Our visualization of melanoma, for example, shows that midline lesions are more aggressive. This is well known by the melanoma specialists at M.D.Anderson, but not known by several dermatologists we consulted.

About six middle- and high-school classes from around Texas were sufficiently stimulated after seeing only a few minutes of our interactive visualization to use all of a half-hour question-and-answer session to explore ramifications of the idea. They asked about the risks of oral cancer, smokeless tobacco, second hand smoke, other drugs and alcohol, cumulative effects, etc. It is well known that gruesome pictures about what can happen if you get cancer are not effective in preventive education. Teens simply deny that anything so terrible could happen to them. After all, everyone knows several healthy smokers. Maybe because our visualization is like a computer game with intriguing diagrams, it can more easily start teens thinking about the processes that underlie these trends.

P.I. was an invited speaker at the First Asia/Pacific Congress on Head and Neck Cancer in Bombay, India in December 1997. The talk resulted in a partially funded trip to New Zealand to continue the work.

The interactive visualization was used in classes at both the U.T. Dental Branch (to teach dental students about oral cancers) and at the M.D.Anderson-Cancer Center (as an example of modern medical informatics).

As the grant ends, pilot studies on the use of this technology to teach dental hygienists about the prevention of oral cancers, have just begun.

Summary and Conclusions:

This project has been a greater success than we anticipated. We accomplished our goal and added visualizations of two additional forms of cancer. Reactions to our work from people all over the world have been positive.

CHRONOLOGICAL APPENDIX

- October 1996: We were notified of the award, hired a programmer, and drafted detailed specifications for the program. Although we originally proposed to use NASA's Fortran Device Independent Graphics Library for this work, it became clear that there was now a better choice. Java - an object-oriented, device-independent, Web-based language - had just been released. We recognized that Java contained many of the features that had attracted us to the NASA libraries - reusable, portable code. The NASA libraries had been sold to Object Access Inc, and were marketed as the Programmers Reusable Library. Worldwide enthusiasm at the time we started this project indicated we would be wiser to write our reusable objects in Java not Fortran. It was a fortuitous decision.
- November 1996: An initial prototype Java visualization was prepared.
- December 1996: The visualization was improved to show the locations of the primary tumors. Experienced surgeons viewed the program and stated it was consistent with their expectations
- January 1997: An introduction to the visualization was added. Our Committee for the Protection of Human Subjects approved the final product. The product was made available over the World-Wide-Web from our home page <http://oto.med.uth.tmc.edu>.
- February 1997: We started getting comments from patients about our Web site. The P.I. was notified of a Fulbright Fellowship to collect data on head and neck cancer in Asia. We planned to prepare similar visualizations of these data to show physicians in developing countries about the specific patterns of disease in their patients.
- March 1997: Our Web site is getting over 80 "hits" a month from all over the world. We participated in a distance learning exercise. A multimedia program originating from Rice University reached multiple middle and high schools between Houston and the Mexican border. The interactive visualization attracted the interest of the students as an entire half-hour, question-and-answer session was devoted to the risks of oral cancer.
- April 1997: We started working on melanoma data. Melanoma is the most rapidly increasing neoplasm in US, especially in southern states with much sun, such as Texas.
- May 1997: We obtained statistical significance in a mapping of metastases from melanoma. We worked to prepare the first-ever use of the Internet in a lecture at our Dental School that featured the interactive visualization of head and neck cancer.
- June 1997: A visualization of the melanoma was prepared.
- July 1997: P.I. left for the Fulbright Fellowship. The visualization was displayed to interested public health officials in Malaysia. The programmer produced a finer analysis of the melanoma data.
- August 1997: The programmer worked to refine the melanoma analyses. The P.I. started collecting data on head and neck metastases in Pakistan.
- September 1997: P.I. continued the research in Pakistan. Additionally a Pakistani colleague offered a set of data on metastases from breast cancer. The programmer produced an important mathematical proof about finding the location of the primary tumor in the coordinates defined by the secondary sites.

October 1997: Analysis of the Pakistani data confirmed that there were significantly different patterns of head and neck metastases compared to Texas. Analysis of the breast-cancer data produced a statistically significant functional map. The programmer performed a thorough statistical analysis of the skin-cancer model.

November 1997: P.I. moved on to India, which has the world's highest rate of head and neck cancer, and continued collecting data for maps of cancer. Indian colleagues also provided data that were used to make maps of cancers in mice and of tuberculosis in AIDS patients. The programmer started working on a visualization of the breast cancer data.

December 1997: The results from this work, and pictures of the visualization were enthusiastically received by delegates at the first Asia/Pacific Congress on Head and Neck cancer held in Bombay. P.I. received an invitation to come to New Zealand for a similar collaboration. The programmer produced an updated visualization of the melanoma data.

January 1998: P.I. moved on to Egypt. A report on the Pakistani breast cancer data was prepared.

February 1998: The programmer produced a general program that could be used to prepare visualizations of any disease.

March 1998: P.I. came back to America through France and England where new data on head and neck metastases were obtained.

April 1998: A report on the English head and neck cancer data was prepared.

May 1998: Data on different patterns of head and neck cancer in elderly Americans were reanalyzed.

June 1998: A report on the mapping of mouse data was prepared.

July 1998: The grant ended. We spent the last few dollars on a new CPU and Microsoft's new implementation of the Java language (J++) to improve our ability to prepare other visualizations. We also made a matched contribution toward the ticket to New Zealand.

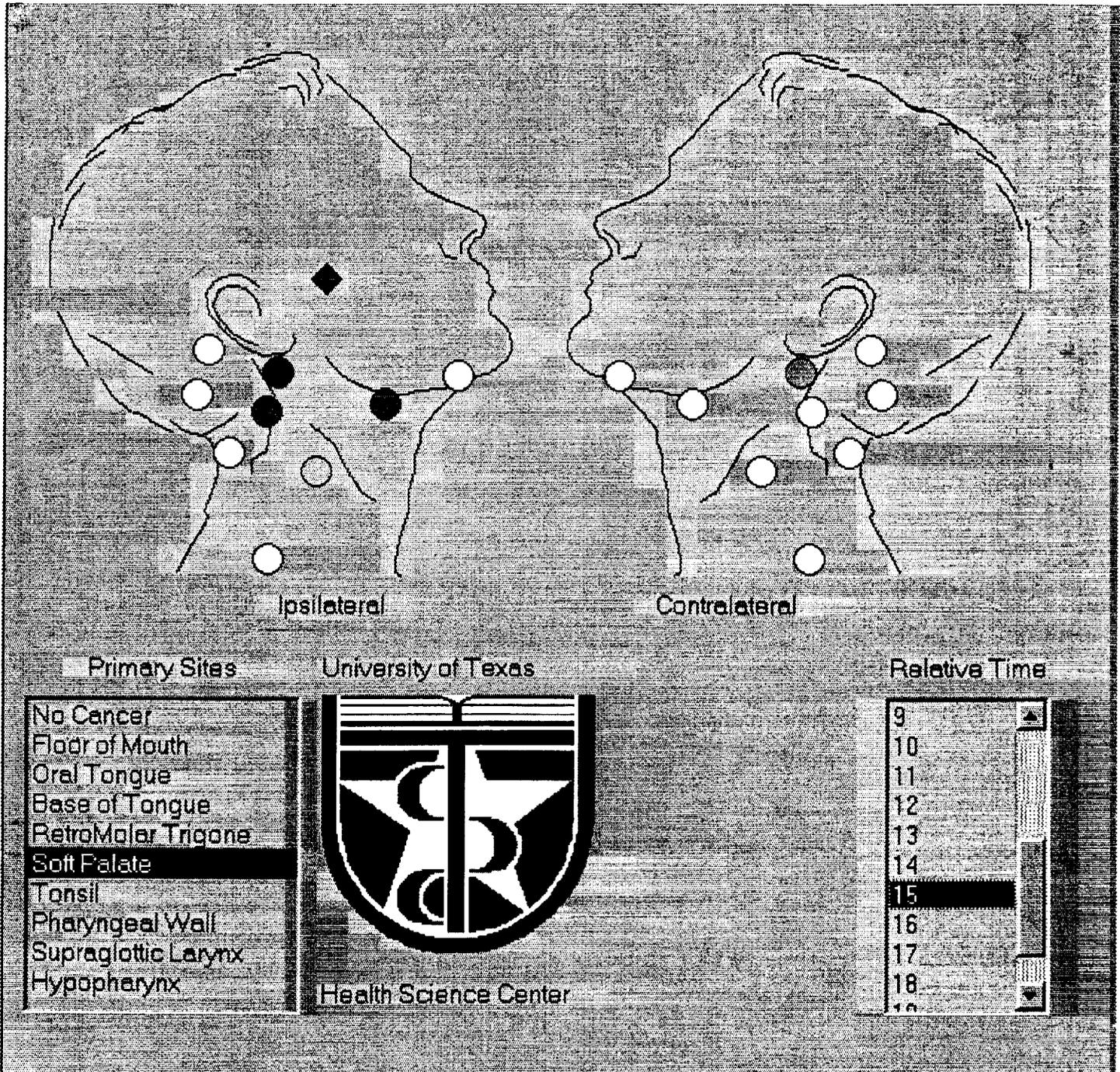
The Future: We have two test sites where, with donated computers, we have been able to put our new software in Dental Hygiene schools. Dental hygienists are in an ideal position to detect early stages of oral cancer and to work toward educating their patients about the risks of this disease. They will make the first steps in using our program to educate themselves and their patients about this deadly disease.

PICTORIAL APPENDICES

Oral Cancers: This initial visualization was the goal of this project. Depicted trends are consistent with experienced surgeons expectation.

Melanoma: See the difference between lateral and midline trunk lesions.

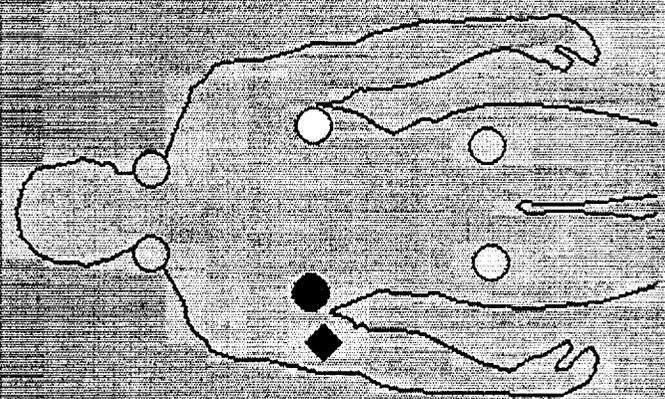
Breast Cancer: Our most recent visualization is shown here in two forms. In the top view anatomically realistic regions change color to depict predicted metastases. The bottom view shows the calculations of an expanding ellipse in the space of the functional map where distances between different regions of the body are NOT related to physical distances.



Gray, Lincoln Clifton

Appendix 7: Example of interactive visualization available at

<http://oto.med.uth.tmc.edu>



Ipsilateral

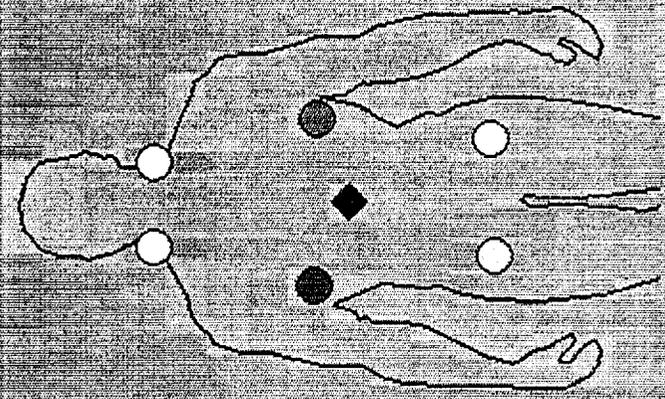
Contralateral

Primary Sites

- No Cancer
- Head/Neck
- Upper Extremity**
- Lateral Trunk
- Lower Extremity
- Mid-Line Trunk

Relative Time

- 11
- 12**
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20



Ipsilateral

Contralateral

Primary Sites

- No Cancer
- Head/Neck
- Upper Extremity**
- Lateral Trunk
- Lower Extremity

Relative Time

- 9
- 10
- 11**
- 12
- 13
- 14
- 15
- 16
- 17

Human Display Bar Chart Overview Abstract Map

Select Primaries by clicking on them in the figure or in the list



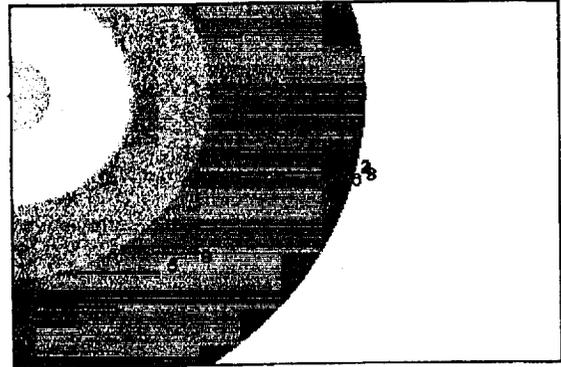
Please choose a Primary Relative time of spread

upper outer
upper inner



Human Display Bar Chart Overview Abstract Map

A dimension in which spread is instantaneous has been omitted



- 1: axilla
- 2: bone
- 3: liver
- 4: lung
- 5: lymph
- 6: skin
- 7: supraClavouli
- 8: blood Vessels

Please choose a Primary Relative time of spread

upper outer
upper inner

